SLC40A1 gene

solute carrier family 40 member 1

Normal Function

The *SLC40A1* gene provides instructions for making a protein called ferroportin. This protein is involved in the process of iron absorption in the body. Iron from the diet is absorbed through the walls of the small intestine. Ferroportin then transports iron from the small intestine into the bloodstream, and the iron is carried by the blood to the tissues and organs of the body. Ferroportin also transports iron out of specialized immune system cells (called reticuloendothelial cells) that are found in the liver, spleen, and bone marrow. The amount of iron absorbed by the body depends on the amount of iron stored and released from intestinal and reticuloendothelial cells.

Research suggests that the amount of ferroportin available to transport iron out of cells is controlled by another iron regulatory protein, hepcidin. Hepcidin binds to ferroportin and causes it to be broken down when the body's iron supplies are adequate. When the body is lacking iron, hepcidin levels drop and more ferroportin is available to bring iron into the body and to release it from storage.

Health Conditions Related to Genetic Changes

African iron overload

Some studies have indicated that a particular variation in the *SLC40A1* gene slightly increases the risk of increased iron stores in people of African descent, which may lead to African iron overload. This effect seems to be more pronounced in men, which may be related to gender differences in the processing of iron.

The *SLC40A1* gene variation associated with increased iron stores replaces the amino acid glutamine with the amino acid histidine at position 248 in the ferroportin protein sequence and is written as Q248H or Gln248His. It is found in 5 to 20 percent of people of African descent but is not generally found in other populations. The Q248H variation may affect the way ferroportin helps to regulate iron levels in the body, resulting in an increased risk of African iron overload. People with the variation may inherit an increased risk of this condition, but not the condition itself. Not all people with this condition have the variation in the gene, and not all people with the variation will develop the disorder.

hereditary hemochromatosis

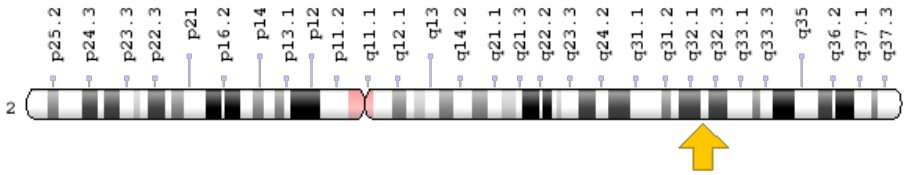
Researchers have identified approximately 15 mutations in the *SLC40A1* gene that cause a form of hereditary hemochromatosis called ferroportin disease, which is also

sometimes referred to as type 4 hemochromatosis. Almost all of these mutations change a single protein building block (amino acid) in ferroportin. Abnormal versions of ferroportin do not permit the normal transport and release of iron from intestinal or reticuloendothelial cells. As a result, the regulation of iron levels in the body is impaired and iron overload results. One mutated copy of this gene in each cell is sufficient to cause ferroportin disease.

Chromosomal Location

Cytogenetic Location: 2q32.2, which is the long (q) arm of chromosome 2 at position 32.2

Molecular Location: base pairs 189,560,590 to 189,580,811 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- Ferroportin 1
- FPN1
- HFE4
- IREG1
- Iron regulated gene 1
- Iron-regulated transporter 1
- MTP1
- S40A1_HUMAN
- SLC11A3
- Solute carrier family 11 (proton-coupled divalent metal ion transporters), member 3
- solute carrier family 40 (iron-regulated transporter), member 1

Additional Information & Resources

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SLC40A1%5BTIAB%5D%29+OR+%28%28Ferroportin+1%5BTIAB%5D%29+OR+%28FPN1%5BTIAB%5D%29+OR+%28HFE4%5BTIAB%5D%29+OR+%28IREG1%5BTIAB%5D%29+OR+%28Iron+regulated+gene+1%5BTIAB%5D%29+OR+%28Iron-regulated+transporter+1%5BTIAB%5D%29+OR+%28MTP1%5BTIAB%5D%29+OR+%28SLC11A3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- SOLUTE CARRIER FAMILY 40 (IRON-REGULATED TRANSPORTER), MEMBER 1
  http://omim.org/entry/604653

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SLC40A1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SLC40A1%5Bgene%5D
- HGNC Gene Family: Solute carriers
  http://www.genenames.org/cgi-bin/genefamilies/set/752
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10909
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/30061
- UniProt
  http://www.uniprot.org/uniprot/Q9NP59

Sources for This Summary

- Beutler E, Hoffbrand AV, Cook JD. Iron deficiency and overload. Hematology Am Soc Hematol Educ Program. 2003:40-61. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14633776
- Beutler E. Hemochromatosis: genetics and pathophysiology. Annu Rev Med. 2006;57:331-47. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16409153

- De Domenico I, Ward DM, Musci G, Kaplan J. Iron overload due to mutations in ferroportin. Haematologica. 2006 Jan;91(1):92-5. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16434376
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3718253/
- De Domenico I, Ward DM, Nemeth E, Vaughn MB, Musci G, Ganz T, Kaplan J. The molecular basis of ferroportin-linked hemochromatosis. Proc Natl Acad Sci U S A. 2005 Jun 21;102(25):8955-60. Epub 2005 Jun 13.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15956209
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1157058/
- Deicher R, Hörl WH. New insights into the regulation of iron homeostasis. Eur J Clin Invest. 2006 May;36(5):301-9. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16634833
- Devalia V, Carter K, Walker AP, Perkins SJ, Worwood M, May A, Dooley JS. Autosomal dominant reticuloendothelial iron overload associated with a 3-base pair deletion in the ferroportin 1 gene (SLC11A3). Blood. 2002 Jul 15;100(2):695-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12091367
- Fleming RE, Sly WS. Ferroportin mutation in autosomal dominant hemochromatosis: loss of function, gain in understanding. J Clin Invest. 2001 Aug;108(4):521-2.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11518724
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC209411/
- Fleming RE. Advances in understanding the molecular basis for the regulation of dietary iron absorption. Curr Opin Gastroenterol. 2005 Mar;21(2):201-6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15711214
- Kelleher T, Ryan E, Barrett S, Sweeney M, Byrnes V, O'Keane C, Crowe J. Increased DMT1 but not IREG1 or HFE mRNA following iron depletion therapy in hereditary haemochromatosis. Gut. 2004 Aug;53(8):1174-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15247188
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1774138/
- McGregor J, McKie AT, Simpson RJ. Of mice and men: genetic determinants of iron status. Proc Nutr Soc. 2004 Feb;63(1):11-20.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15070436
- McKie AT, Barlow DJ. The SLC40 basolateral iron transporter family (IREG1/ferroportin/MTP1). Pflugers Arch. 2004 Feb;447(5):801-6. Epub 2003 Jun 27. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12836025
- McKie AT, Marciani P, Rolfs A, Brennan K, Wehr K, Barrow D, Miret S, Bomford A, Peters TJ, Farzaneh F, Hediger MA, Hentze MW, Simpson RJ. A novel duodenal iron-regulated transporter, IREG1, implicated in the basolateral transfer of iron to the circulation. Mol Cell. 2000 Feb;5(2): 299-309.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10882071
- Pietrangelo A. Hereditary hemochromatosis--a new look at an old disease. N Engl J Med. 2004 Jun 3;350(23):2383-97. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15175440
- Pietrangelo A. Non-HFE hemochromatosis. Semin Liver Dis. 2005 Nov;25(4):450-60. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16315138

- Rivers CA, Barton JC, Gordeuk VR, Acton RT, Speechley MR, Snively BM, Leiendecker-Foster C, Press RD, Adams PC, McLaren GD, Dawkins FW, McLaren CE, Reboussin DM. Association of ferroportin Q248H polymorphism with elevated levels of serum ferritin in African Americans in the Hemochromatosis and Iron Overload Screening (HEIRS) Study. Blood Cells Mol Dis. 2007 May-Jun;38(3):247-52. Epub 2007 Feb 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17276706
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727273/
- Thomas C, Oates PS. Ferroportin/IREG-1/MTP-1/SLC40A1 modulates the uptake of iron at the apical membrane of enterocytes. Gut. 2004 Jan;53(1):44-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14684575
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1773934/
- Wallace DF, Pedersen P, Dixon JL, Stephenson P, Searle JW, Powell LW, Subramaniam VN. Novel mutation in ferroportin1 is associated with autosomal dominant hemochromatosis. Blood. 2002 Jul 15;100(2):692-4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12091366
- Zaahl MG, Merryweather-Clarke AT, Kotze MJ, van der Merwe S, Warnich L, Robson KJ. Analysis of genes implicated in iron regulation in individuals presenting with primary iron overload. Hum Genet. 2004 Oct;115(5):409-17. Epub 2004 Aug 24.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15338274

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/SLC40A1

Reviewed: October 2012
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services